IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA

PATRICK KELLETT, JOHN O'MARA, DANIEL MURPHY, ELMO O'NEAL, MARK MORGAN, MICHAEL JARRELL, JAMES MURPHY, HANFORD GROSS, JOSEPH BEETZ, and ROBERT MITCHELL In Their Representative Capacities as Trustees of the PLUMBERS AND PIPEFITTERS WELFARE EDUCATION FUND,	)	CV 08 3668 CRB
Plaintiffs	)	Civil Action No. _____
v.	)	JURY TRIAL DEMANDED
	)	MDL #1699
PFIZER, INC., PHARMACIA CORPORATION, AND G.D. SEARLE LLC., Defendants.	)	

COMPLAINT

1. Plaintiff Plaintiff Plumbers and Pipefitters Welfare Education Fund through its Trustees, brings this action individually against Defendants, Pfizer, Inc. ("Pfizer"), Pharmacia Corporation ("Pharmacia"), and G.D. Searle & Co. ("Searle"), to recover damages, restitution, refunds, and/or for equitable relief arising from its payments made between November 16, 2001, and April 7, 2005, with respect to the prescription drug Bextra ("Bextra"), an anti-inflammatory drug researched, manufactured, marketed, promoted, advertised, sold and distributed by a combination and/or collaboration of said Defendants.

PARTIES

2. Plaintiff, Plumbers and Pipefitters Welfare Educational Fund ("Welfare Fund") is an employee benefit plan within the meaning of Sections 3(1) and (3) 502 and 515 of ERISA, 29 U.S.C. §§ 1002(1), (3), 1132 and 1145. Plaintiffs Kellett, O'Mara, Murphy, O'Neal, Morgan, Jarrell, Murphy, Gross, Beetz and Mitchell ("Trustees") are the duly designated Trustees of the

Pension Fund and are fiduciaries within the meaning of Section 3(21)(A) and 502 of the Employee Retirement Income Security Act of 1974 ("ERISA"), 29 U.S.C. §§1002(21)(A) and 1132. The Welfare Fund is administrated from offices located at 12385 Larimore Rd., St. Louis, Missouri 63138.

3. Defendant Pfizer is a Delaware corporation with its principal place of business in New York. In 2003, Pfizer acquired Pharmacia for nearly $60 billion. During the relevant time period, Pfizer has been engaged in the business of marketing and selling Bextra nationwide. Defendant Pfizer may receive service of process through its Registered Agent: CT Services Corporation, 818 W. 7th Street, Los Angeles, CA 90017.

4. Defendant Pharmacia is a Delaware corporation with its principal place of business in New Jersey. At all relevant times, Pharmacia has been engaged in the business of marketing and selling Bextra nationwide. Defendant Pharmacia may receive service of process through its Registered Agent: CT Services Corporation, 818 W. 7th Street, Los Angeles, CA 90017

5. Defendant Searle is a Delaware corporation with its principal place of business in Illinois. At all relevant times, Searle has been engaged in the business of marketing and selling Bextra nationwide. Defendant Searle may receive service of process through its Registered Agent: CT Services Corporation, 818 W. 7th Street, Los Angeles, CA 90017.

JURISDICTION

6. There is complete diversity of citizenship between Plaintiff and Defendants. Additionally, the amount in controversy exceeds $75,000, excluding costs and interest. Therefore, this Court has jurisdiction of this matter under 28 U.S.C. 1332.

7. Venue is proper in this District pursuant to 28 U.S.C. § 1391(a) because defendants are subject to personal jurisdiction in this judicial district.

SUMMARY OF ALLEGATIONS

8. Non-steroidal anti-inflammatory drugs (NSAIDs") have been widely used to treat arthritis, acute and chronic pain for nearly forty (40) years. The pain relief offered by such NSAIDs comes at the expense of important adverse effects, most notably upper gastrointestinal toxicity. Use of NSAIDs leads to admission to hospital for ulcer complications (bleeding and perforation) in approximately one percent (1%) of users annually and results in thousands of deaths every year.

9. In 1989, scientists made a breakthrough in understanding how NSAIDs worked. Cyclo-oxygenase, the enzyme inhibited by NSAIDs, exists in at least two forms in the body. Traditional NSAIDs inhibit both the cyclo-oxygenase 2 ("COX-2") enzyme, which is inducible and expressed at sites of inflammation, and the COX-1 enzyme, which is constitutive and expressed in the gastrointestinal ("GI") system. Inhibition of the COX-2 enzyme decreases inflammation and alleviates pain. Inhibition of the COX-1 enzyme, however, decreases the protection in the GI tract. Defendants leapt at this new understanding, hoping to create a new breed of NSAID that alleviated pain, but did not have the toxicity associated with traditional NSAIDs.

10. Bextra was one of the new COX-2 inhibitors. Vioxx and Celebrex are others. Defendants believed that Bextra had the potential to be a new blockbuster drug with yearly sales in the billions of dollars.

11. As part of the unlawful scheme set forth below, Defendants promoted the use of Bextra in information disseminated to doctors, Pharmacy Benefit Managers ("PBMs"), third-party payors and consumers. Defendants promoted Bextra as a "breakthrough" drug providing important clinical advantages over older and far less expensive NSAIDs. Defendants were never able to establish, however, that Bextra was any more efficacious or safer than traditional

NSAIDs. To the contrary, studies showed risks for gastrointestinal and cardiovascular ("CV") adverse event rates similar to or greater than traditional NSAIDs. The FDA approved label warned of GI and CV risks similar to other NSAIDs. Even so, as part of the unlawful scheme set forth below, Defendants embarked on a massive marketing campaign directed to doctors, third party payors and consumers to market Bextra as a "Powerful" drug clinically superior to and safer than older and far less expensive NSAIDs.

12. Defendants falsely represented that Bextra provided symptomatic relief similar to ibuprofen and naproxen but was clinically superior because it was significantly less likely to cause the gastrointestinal adverse side effects associated with these and other NSAIDs. For instance, NSAIDs can, in certain patients, cause gastrointestinal perforations, ulcers and bleeding with long-term use. Defendants falsely promoted Bextra as a safe and effective alternative that would have less deleterious and painful impact on the gut, but that would be just as effective, if not more so, for pain relief.

13. The extent to which a drug is paid for by third-party payors, such as the Welfare Fund, is determined by that drug's status on the third-party payor's "formulary," which is a list of drugs that plan participants are authorized to purchase for payment under the benefit plan.

14. Placement of a prescription drug on the formularies of third-party payors, medical care organizations, and/or prescriptions benefit managers (who are employed by third-party payors to design or administer the benefit plans) is critical to the success of the drug. Defendants knew that preferred placement on these formularies would guarantee commercial success for Bextra.

15. In an elaborate and sophisticated manner, Defendants aggressively marketed Bextra directly to medical professionals (including physicians, dentists, and leading medical scholars) in order to leverage pressure on third-party payors, medical care organizations, and

large institutional buyers (e.g. hospitals) to include Bextra on their formularies. Bextra's marketing campaign specifically targeted third-party payors, physicians and dentist, and was designed to convince them both of the therapeutic and economic value of Bextra. Faced with the increased demand for the drug by health care professionals that resulted from Bextra's successful advertising and marketing blitz, third-party payors were compelled to add Bextra to their formularies.

16. Defendants' marketing and promotion of Bextra was part of a scheme to create the impression of, and demand for, Bextra as a wide-ranging pain reliever, particularly for the treatment of arthritis pain and/or pain in general (a use for which it was not FDA approved). The scheme was accomplished by unlawful means including, but not limited to, the (i) false promotion, including promotion contrary to the FDA approved label, of the overall efficacy and safety of Bextra as superior to less expensive alternatives, (ii) false promotion, including promotion contrary to the FDA approved label of the CV and GI safety of Bextra (iii) manipulation of data to give the appearance of superiority over other NSAIDs in pain relief efficacy, CV and GI safety when such superiority did not exist and was contrary to the FDA approved label, directed to doctors, third-party payors and consumers, touting the superior efficacy and GI and CV safety of Bextra, which promotions exceeded the scope of FDA approval, (v) use of reprinted articles from prestigious medical journals that falsely claimed Bextra was proven to be safer than other NSAIDs contrary to the FDA approved label and (vi) co-promotion of Bextra with Celebrex in an attempt to convince doctors incorrectly that the alleged benefits of one drug applied to both even though such claims were contrary to the FDA approved label of each drug.

17. As a result of Defendants' scheme, they were able to create a market for Bextra and to sell Bextra at a premium price over NSAIDs and to have it become a standard treatment

option in many circumstances as opposed to use of less expensive NSAIDs. Bextra sales reached $1.29 billion in 2004.

18. The success of Defendants' scheme was recently documented in a study released on January 24, 2005, in the ARCHIVES OF INTERNAL MEDICINE, Volume 165, entitled *National Trends in Cyclooxygenase-2 Inhibitor Use Since Market Release*. The authors of that study concluded that the "aggressive marketing techniques to patients and physicians" caused a growth not only in us of COX-2 inhibitors but also in overall market demand, resulting in the use of such drugs for patients who did not need them.

19. In fact, Bextra has been promoted as a superior pain reliever when for most patients it has no proven superiority over other NSAIDs. To date there are ***no*** clinical studies that demonstrate an advantage of Bextra over other NSAIDs that would offset concerns about serious skin risks (e.g., toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme), such as studies showing a GI safety benefit compared to other products. In addition, Bextra has been documented to be associated with increased risk of serious adverse cardiovascular events to such an extent, that on April 7, 2005, the Federal Drug Administration ("FDA") requested Pfizer to withdraw Bextra from the United States market and Pfizer has done so. At the FDA briefing called to explain its request that Pfizer withdraw Bextra from the market, the FDA's director of the Office of New Drugs said that Bextra "had no unique benefit and it had the unique risk: the skin reaction"[1]

20. At all times relevant, Bextra sold for $2.53 to $6.45 per day depending upon the dose, while NSAIDs sold for as little as $0.21 to $0.31 per day. Billions of dollars have thus been wasted in which Plaintiff have paid a premium price for a drug (and the doctor visits necessary to obtain prescriptions for Bextra) that is not a premium or superior product over

[1] Rita Rubin, "Another drug for pain off market," *USA Today*, 4/7/2005.

equally available, less expensive NSAIDs and other pain medications. If Defendants had not engaged in the wrongful marketing, advertising and promotion of Bextra, Plaintiff would have paid for other, equally effective and less expensive medications or would have purchased no medication at all. Had the truth been told about its safety and efficacy, Bextra would have sold at a price similar to that of other NSAIDs and would not have become a standard in the treatment of arthritis, dysmenorrheal and other non-FDA approved forms of pain relief, and/or Bextra would not have been marketed at all and would not have been approved on formularies. The plain fact is that at no time did Bextra, as compared to other equally effective and less expensive therapeutic regimens, have a proven advantage for patients either at no risk or at high risk for GI complications. Thus, for virtually every purchaser – and contrary to Defendants' widespread marketing program – Bextra was neither more effective nor safer than older, less expensive NSAIDs and thus was not a superior product.

21. In this action Plaintiff seek damages arising from its purchases of Bextra resulting from Defendants' illegal scheme and/or conduct.

FACTUAL BACKGROUND

A. Development of Bextra

22. Bextra is one of the new entries in a class of pain medications called non-steroidal anti-inflammatory drugs ("NSAIDs"). Aspirin, naproxen and ibuprofen are examples of well-known NSAIDs.

23. NSAIDs reduce pain by blocking the body's production of pain transmission enzymes called cyclo-oxygenase or "COX." There are at least two forms of COX enzymes relevant to NSAIDs, COX-1 and COX-2.

24. COX-1 is constitutively expressed in most tissues throughout the body, including the gastrointestinal tract, kidneys and platelets.

25. COX-2 is inducible, and is normally found in very low amounts in health tissue (except the brain and kidney) but is prominently expressed in inflamed tissues. COX-2 is not expressed in the platelets or gut.

26. It is generally accepted in the medical community that blocking the COX-1 enzyme hampers the body's ability to repair gastric tissue and causes harmful gastrointestinal side effects, including stomach ulceration and bleeding. In addition, blocking the COX-1 enzyme decreased the production of thromboxane in platelets, diminishing thromboxane's effect of vasoconstriction and platelet aggregation, and thereby increasing the risk of abnormal bleeding.

27. It is generally accepted in the medical community that selectively blocking the COX-2 enzyme without also blocking the COX-1 enzyme encourages the formation of blood clots and increases the risk of various clot-related cardiovascular events, including heart attack, stroke, unstable angina, and peripheral blood clots.

28. Traditional NSAIDs like aspirin reduce pain sensations by inhibiting both COX-1 and COX-2 enzymes simultaneously. As would be expected, traditional NSAIDs may cause ulcers in the stomach and intestines. However, because of a complex chemical balance in the human body, traditional NSAIDs do not cause blood clots, and aspirin even reduces the risk of clots and helps protect heart function in some people, an effect commonly referred to as "cardioprotection."

29. For decades, in the absence of other treatment options, consumers seeking pain relief were forced to accept and live with the gastrointestinal risks of traditional NSAIDs, counteract the GI effect with other medication, or take nothing and live with the pain.

30. Defendants set out to remedy this problem by developing "selective" inhibitors that would block on COX-2 production, and thus the *theory* – although no the clinically proven

fact – was that this might allow the proper maintenance of gastric tissue while still reducing pain sensations.

31. In making this decision, Defendants either intentionally ignored or recklessly disregarded current medical knowledge that selective COX-2 inhibition lowers prostacyclin levels without counterbalancing reduction in thromboxane production, thereby increasing the risk of blood clots and various clot-related cardiovascular events, including heart attack, stroke, unstable angina and peripheral blood clots.

32. Defendants launched Celebrex, the first of three major selective COX-2 inhibitor drugs, in early 1999 and initiated a massive marketing campaign to convince doctors and consumers of the superiority of the new "blockbuster" drug over less expensive NSAIDs. Merck & Co., Inc. ("Merck") launched Vioxx shortly thereafter and engaged in similarly deceptive advertising and marketing of its new COX-2 inhibitor.

33. Defendants sought approval of a second generation COX-2 inhibitor and filed for FDA approval of Bextra (Valdecoxib) on January 16, 2001 for the (i) prevention and treatment of acute pain, (ii) treatment of primary dysmenorrheal, and (iii) relief of the signs and symptoms of osteoarthritis and adult rheumatoid arthritis.

34. In its pre-approval marketing plans, Defendants assumed that Bextra would be approved and that such approval would include an indication that it was safer than other NSAIDs in protecting against GI complications. The treatment of pain with reduced GI complications was the single most important attribute to the planned marketing and promotion of Bextra and its place a new blockbuster drug.

35. Pre-approval marketing plans were to stress that Bextra was superior to other NSAIDs in terms of both efficacy and safety, offering a significant reduction in GI

complications. Pre-approval marketing plans also anticipated that the FDA would approve Bextra for the treatment of acute pain in adults.

36. In September 2000, Defendants submitted a new drug application for an injectible COX-2, generically named "parecoxib" (a "pro-drug" of Bextra that gets metabolized immediately into Bextra after its administration). In July 2001, the FDA declined to approve parecoxib. In the disapproval letter, the FDA states:

> The safety of parecoxib in the multiple dose setting has not been adequately established. Findings in Study 035 raise the possibility that parecoxib is associated with serious, life-threatening adverse events including myocardial infarction, thrombo-embolic events (such as cerebrovascular accidents, deep venous thrombosis and luminary embolism), pericarditis, upper gastrointestinal injury, and hypotension. Hypoxia, renal dysfunction and hypertension were also experience more frequently with parecoxib use than the comparator analgesic. All four death in the study occurred in the parecoxib treated group.

Defendants ignored this clear cardiovascular signal with a drug almost identical to Bextra and continued their deceptive launch plans.

37. The FDA granted approval of Bextra on November 16, 2001 for two particular uses: treatment of primary dysmenorrhea and relief for the signs and symptoms of osteoarthritis and rheumatoid arthritis.

38. However, the agency did not grant approval of Bextra for the management or prevention of acute pain. In rebuking the effort to obtain such a broad indication for Bextra, the FDA determined that Bextra had not been proven as more effective than other NSAIDs, and that given the ongoing concerns regarding COX-2s generally at that time, broader indications in that class should not be granted. Further, Defendants did not obtain approval to promote Bextra as less likely than other NSAIDs to cause clinically serious GI events, a potentially serious blow to Defendants. As a result, the Bextra package inserts had to include a warning that its use presented "risk of GI ulceration, bleeding, and perforation."

39. The FDA also warned that Bextra had not demonstrated safety and efficacy for opiod sparing, noting,

> ...adverse events associated with opiods such as hypotension were seen more frequently in the Valdecoxib treated patients. There was no clear evidence of less confusion, somnolence, respiratory depression, nausea and vomiting or constipation to suggest a clinical benefit of post-operative co-administration of fixed dosing of Valdecoxib and ad lib opiod dosing has not been demonstrated.

As described in detail below, Defendants ignored these warnings and limitations on the indications for Bextra and falsely touted it as a powerful pain reliever with opiod sparing benefits.

40. The original label for Bextra also contained the following precautions relating to the cardiovascular risks associated with Bextra:

> **Renal Effects**
>
> Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in the administration of a nonsteroidal anti-inflammatory drug may cause a dose-dependent reduction in prostaglandin formation and, secondarily, in renal blood flow, which may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and Angiotensin Converting Enzyme (ACE) inhibitors, and the elderly.
>
> ...
>
> **Fluid Retention and Edema**
>
> Fluid retention and edema have been observed in some patients taking BEXTRA (see ADVERSE REACTIONS). Therefore, BEXTRA should be used with caution in patients with fluid retention, hypertension, or heart failure.

The label warned of particular interactions with other medicines, including,

> ***Aspirin***: Concomitant administration of aspirin with Valdecoxib may result in an increased risk of GI ulceration and complications compared to valdecoxib alone. Because of its lack of anti-platelet effect Valdecoxib is not a substitute for aspirin for cardiovascular prophylaxis.

The ADVERSE REACTIONS section of the original label warned that adverse CV events including, aggravated hypertension, aneurysm, angina pectoris, arrhythmia, cardiomyopathy, congestive heart failure, coronary artery disorder, heart murmur, hypotension, bradycardia, palpitation, and tachycardia had been observed in patients treated with Bextra.

41. Even though the Defendants were required to market Bextra only as described in the FDA approved label, they marketed Bextra's safety and efficacy as far superior than the information that appeared in its labeling. For example, in a February 2002 letter from the FDA to Pharmacia, the FDA reviewer found multiple misleading claims in the launch advertisements submitted. The FDA warned, "[y]our proposed detail aid is misleading because it contains claims that overstate the effectiveness of Bextra" and stated that claims made in the same detail aid were "misleading because these efficacy claims have not been demonstrated by substantial evidence."

42. In the same letter, the FDA reviewer specifically criticized Pharmacia's "misleading presentations" including, (1) presentation of data that had not been sufficiently replicated, (2) selective presentation of the most positive results and failure to include results that were not favorable, (3) presentation of data from a prospective subgroup analysis, when the original study did not contemplate analysis of the data in such subgroups, falsely producing positive results, (4) pooling of data from trials that were not designed with the endpoints the defendants presented, (5) use of theoretical models that had not been demonstrated by substantial evidence, (6) unbalanced presentation of benefits versus risks, specifically, portraying benefits in bold, large type at the top of the ad and risks in small, light type at the bottom of the ad. Although Defendants were provided this direction prior to the launch of Bextra, they ignored it and proceeded to use all of the above misleading marketing techniques throughout Bextra's reign in the market.

43. Almost three years later, in January 2005, the FDA continued to criticize Defendants misleading marketing methods. In response to submitted promotional pieces for Bextra and Celebrex, the FDA commented generally,

> [t[hese five promotional pieces variously: omit material facts, including the indication and risk information; fail to make adequate provision for the dissemination of the FDA-approved product labeling; and make misleading safety, unsubstantiated superiority, and unsubstantiated effectiveness claims. They are, therefore, in violation of the Federal Food, Drug and Cosmetic Act (Act) and FDA implementing regulations.

The letter pointed out that a particular advertisement, "arthritis tips TV ad" was not even submitted to the FDA as required by federal regulations. The letter went on to warn,

> [s]pecific warnings related to: gastrointestinal (GI) effects, including risks of GI ulceration, bleeding and perforation; hypersensitivity reactions including anaphylactoid reactions and angioedema; use in patients with advanced renal disease, due to lack of controlled clinical studies regarding use of the products in this population; and use in patients with preexisting asthma.

The letter concluded that the violations it discusses are of a "serious nature" and Defendants should "act to avoid disseminating similarly misleading promotion[s] ...in the future." The Defendants are further warned that the violations discussed in the letter are not an "exhaustive list" and that [i]t is [Defendants'] responsibility to ensure that your promotional materials for Celebrex and Bextra comply with each applicable requirement of the Act and FDA implementing regulations."

44. Defendants responded that they disagreed with the FDA's interpretation of the advertisements. Instead of immediately halting the advertisements or the misleading methods highlighted by the FDA, the Defendants explicitly told the FDA that they would "consider DDMAC's comments" when developing advertisements in the future.

B. Studies on Bextra and Other COX-2 Inhibitors

45. Based on studies performed on Celebrex, Vioxx, Bextra, and other COX-2 inhibitors, Defendants knew by 1998 that selective COX-2 inhibitors posed serious cardiovascular risks for anyone who took them, and presented a specific additional threat to anyone with existing heart disease or cardiovascular risk factors.

46. For example, in an effort to demonstrate that Celebrex had greater gastrointestinal safety than traditional NSAIDs, Defendants funded a clinical trial, the results of which were published in 2000: the Celecoxib Long-Term Arthritis Safety Study ("CLASS"). Defendants expected CLASS to show that Celebrex produced significantly fewer serious GI complications than traditional NSAIDs.

47. The CLASS trial was a long-term, double-blind study of gastrointestinal toxicity in 8,059 patients taking Celebrex, ibuprofen, or diclofenac to treat arthritis. Patients with heart problems were allowed to participate in the CLASS trial, and were permitted to take low doses of aspirin to reduce the risk that they would suffer an adverse cardiovascular event during the study.

48. When the CLASS study was completed, the results were reported to the U.S. Food and Drug Administration's Arthritis Drugs Advisory Committee (the "Committee") as part of a request to exempt Celebrex from including a gastrointestinal safety warning in its package insert. After reviewing the CLASS results, however, the Committee concluded that patients taking Celebrex had not experienced fewer gastrointestinal complications than those taking traditional NSAIDs. Moreover, the CLASS study demonstrated a trend toward cardiovascular risks for those taking the selective COX-2 inhibitor Celebrex.

49. A post hoc analysis and comparison of CLASS study patients taking low-dose aspirin for cardiac protection and patients not taking low-dose aspirin revealed that the rate of

combined anginal adverse events was 1.4% in the celecoxib (Celebrex) group versus 1.0% in the ibuprofen and diclofenac groups. Although not a statistically significant difference, this tendency towards increased cardiovascular toxicity was described by the FDA Medical Officer Dr. Witter, who stated that "[f]or anginal disorders (especially the combined disorders), there seems to be a trend toward more [cardiac adverse] events in those patients receiving celecoxib, regardless of aspirin use."

50. This trend was magnified in those patients not taking low-dose aspirin. Combined anginal disorders were increased in these patients; the celecoxib group had 0.6% vs.0.2% and 0% in the diclofenac and ibuprofen groups, respectively. There were also more combined atrial serious cardiac adverse events with celecoxib, 0.3% compared to 0.1% and 0% in the diclofenac and ibuprofen groups, respectively. Dr. Witter commented that "[i]n the non-aspirin users, there appears to be a slight trend toward more [serious cardiac adverse] events in those patients receiving celecoxib for combined atrial and anginal disorders." Additionally, the rate of myocardial infarction was higher in the celecoxib group, 0.2%, compared with the other two drugs, 0.1%. Dr. Witter also referred to data from the original New Drug Application ("NDA") for celecoxib in his discussion, stating that "[t]here were suggestions of a dose-response relationship (...100 mg BID celecoxib, 0% crude mortality rate vs. 400 mg BID celecoxib, 0.64% crude mortality rate) between cardiovascular mortality and [increased] celecoxib use that could not be adequately addressed by the data."

51. The FDA was concerned enough that they ordered a cardiorenal consult by Medical Officer Dr. Throckmorton on the same CLASS study data. In his report he noted, "[t]he CLASS trial data do not support a large adverse effect of celecoxib on cardiovascular mortality or on serious adverse events related to thrombosis relative to either diclofenac or ibuprofen. The

data do not exclude a less apparent pro-thrombotic effect of celecoxib, such as might be reflected in the relative rates of cardiac adverse events related to ischemia."

52. While none of the CLASS data was statistically significant, they revealed a consistent and worrisome trend toward increased cardiovascular toxicity, particularly with regard to increased thrombosis.

53. While none of the CLASS data was statistically significant, they revealed a consistent and worrisome trend toward increased cardiovascular toxicity, particularly with regard to increased thrombosis.

54. Importantly, the reviewers recommended that "[o]ur findings suggest a potential increase in cardiovascular event rates for the presently available COX-2 inhibitors... definitive evidence of such an adverse effect will require a prospective randomized clinical trial.. Given the remarkable exposure and popularity of this new class of medications, we believe that it is mandatory to conduct a trial specifically assessing cardiovascular risk and benefit of these agents. Until then, we urge caution in prescribing these agents to patients at risk for cardiovascular morbidity." Although employing a placebo group from a different trial weakens the validity of their analysis, the author's call for a prospective randomized clinical trial powered to truly analyze the cardiovascular risk to benefit ratio was then exactly correct. A subsequent placebo-controlled trial of celecoxib clearly demonstrated this risk.

55. The subsequent trial was the APC colon polyp recurrence prevention study, in which approximately 2000 patients took celecoxib or a placebo. Interestingly, this was the longest celecoxib trial to date with mean duration of treatment being 33 months as opposed to the much shorter 12-month duration of the CLASS study. A statistically significant elevation in the risk of major fatal or non-fatal cardiovascular events (a composite endpoint of cardiovascular death, acute myocardial infarction, and stroke) was seen in those patients taking celecoxib

compared to those in the placebo group. This followed a dose-response relationship: the relative risk at 400 mg/day of celecoxib was 2.5 while the relative risk at 800 mg/day was 3.4. Because of this unacceptable danger, the trial was prematurely halted. The FDA released an explanatory statement which said, "[w]hile we have not seen all available data on Celebrex, these findings are similar to recent results from a study of Vioxx (rofecoxib), another drug in the same class as Celebrex. Vioxx was recently voluntarily withdrawn by Merck."

56. Merck had previously conducted a large-scale, long-term, double-blind study of gastrointestinal toxicity in patients taking Vioxx or naproxen to treat arthritis. This study came to be called the Vioxx Gastrointestinal Outcomes Research study ("VIGOR").

57. Merck designed VIGOR to produce the absolute minimum number of cardiovascular events by excluding patients with (a) a history of heart attack or coronary artery bypass surgery within the past year; (b) a history of stroke or transient ischemic attack within the past two years; or (c) or those who "required or who had been receiving treatment with aspirin," effectively excluding patients with a history of coronary artery or cerebrovascular disease. Despite being designed so that participants would have far less cardiovascular disease than the normal population taking NSAIDs and thereby minimizing the apparent cardiovascular risk of Vi ox x in comparison to naproxen, the VIGOR results still showed that patients taking Vioxx suffered more than twice the number of serious thrombotic cardiovascular events and five times the number of heart attacks as patients taking naproxen.

58. In October 2000, Merck sent its cardiovascular data from the VIGOR trial to the FDA for review. In February 2001, the FDA published a Memorandum on the Vioxx cardiovascular safety data gathered during VIGOR. In this Memorandum, the FDA concluded that there "is an increased risk of cardiovascular thrombotic events, particularly [heart attack], in the [Vioxx] group compared with the naproxen group." The FDA considered and rejected all

defenses raised by Merck to explain the statistically significant increase of cardiovascular incidents among Vioxx users. In February 2001, the FDA also concluded that Merck should have to add a cardiovascular warning to its Vioxx packaging: "it would be difficult to imagine inclusion of VIGOR results in the [Vioxx] labeling without mentioning cardiovascular safety results in the study description as well as the Warnings sections."

59. In August 2001, independent doctors from the Cleveland Clinic performed their own meta-analysis of the Celebrex and Vioxx clinical trials on the issue of cardiovascular safety. Their findings "suggest a potential increase in cardiovascular event rates for the presently available COX-2 inhibitors." Based on their findings and the widespread use of COX-2 inhibitors, these doctors concluded "that it is mandatory to conduct a trial specifically assessing cardiovascular risk and benefit of these agents."

60. In light of these studies and FDA findings, Defendants were well aware of the serious cardiovascular risks posed by selective COX-2 inhibitors, including Bextra, long before Defendants began marketing Bextra as being safe and more effective than traditional NSAIDs for all patients, without regard for cardiovascular risks.

61. Studies show that COX-2 inhibitors, including Bextra, decrease production of a cardioprotective substance called prostacyclin. When prostacyclin synthesis is suppressed the arteries are more vulnerable to clotting, high blood pressure, heart attack, and stroke.

62. Label changes implemented in November 2004 reflected the growing scientific data that Bextra and parecoxib posed serious cardiovascular risks. A contraindication was added for the treatment of post-operative pain immediately following coronary artery bypass graft surgery based on the results of three placebo-controlled studies (two coronary artery bypass graft (CAB G) surgery studies and one general surgery study) that were conducted to evaluate the

safety of Bextra and parecoxib. As reflected in the new labeling, results of the first CABG study ("CABG I") showed,

> a significantly ($p<0.05$) greater incidence of cardiovascular/thromboembolic events (myocardial infarction, ischemia, cerebrovascular accident, deep vein thrombosis and pulmonary embolism)...in the parecoxib/vadecoxib treatment group compared to the placebo/placebo treatment group for the IV dosing period (2.2% and 0.0% respectively) and over the entire study period (4.8% and 1.3% respectively).

CABG I results also revealed an increased rate of surgical wound complications in patients treated with valdecoxib and parecoxib.

63. The results of CABG II, as reflected in the new label, emphasized these cardiovascular risk concerns. CABG II revealed,

> [a] significantly... greater incidence of events in the cardiovascular/thromboembolic category... in the parecoxib/valdecoxib treatment group (2.0%) compared to the placebo/placebo treatment group (0.5%). Placebo/valdecoxib treatment was also associated with a higher incidence of CV thromborembolic events versus placebo treatment, but this difference did not reach statistical significance.

Although the third general surgery study did not reveal significant differences in the overall safety profile of the comparators, the FDA found the data as a whole compelling enough to include the new contraindication for CABG patients in the labeling.

64. Another new addition to the label, entitled "Cardiovascular Safety Analysis from Osteoarthritis and Rheumatoid Arthritis Studies," explains that although "no apparent differences were detected in the exposure-adjusted serious cardiovascular thromboembolic event rates between patients receiving BEXTRA, placebo and NSAIDs," Bextra has not been studied in controlled clinical trials longer than one year and the clinical studies that have been conducted were not powered to detect differences cardiovascular events in a chronic setting.

65. The FDA also required the strengthening of warnings about the risk of life-threatening skin reactions, including Stevens-Johnson Syndrome and toxic epidermal necrolysis. Stevens-Johnson Syndrome is marked by blistering lesions on the body, prone to rupture and secondary infection, and has been described as burning from the inside out. Patients with toxic epidermal necrolysis, also known as TENS, develop multiple large blisters, followed by the sloughing of the skin and mucous membranes.

66. By November 2004, the FDA had received nearly ninety reports of such severe skin reactions, some of which resulted in hospitalization and death. While other NSAIDs also pose a risk for rare, serious skin reactions, the reported rate of such side effects was vastly higher in individuals taking Bextra.

67. In mid-January 2005, an editorial in Circulation combined the results of two studies of Bextra and parecoxib in post-cardiac bypass surgery patients (separate from the studies described above). The results showed that those taking Bextra and parecoxib developed three times more heart attacks and strokes (statistically significant) than those given a placebo.

68. In February 2005, WellPoint, Inc., the nation's largest provider of health care benefits, released a study it conducted in conjunction with researchers at Indiana University's medical school on the risks of cardiovascular events in patients taking COX-2 inhibitors. The study involved the records of more than 635,000 patients and demonstrated that COX-2 inhibitors do increase the risk of adverse cardiovascular events. However, while Vioxx increased patients' risk of heart attack and stroke by approximately 20%, Bextra increased the risk by 50%. Dr. Sam Nussbaum, WellPoint's executive vice president and chief medical officer, noted that the study was further evidence of an "increasingly compelling trend" of data showing that COX-2 inhibitors elevate patients' risk of adverse cardiovascular events.

69. From February 16-18,2005, the FDA's Drug Safety and Risk Management Advisory Committee and the Arthritis Drug Advisory Committee met jointly to further examine the safety ofCOX-2 inhibitors. There, FDA Office of Drug Safety Officer David Graham stated that COX-2 inhibitors increase the risk for adverse cardiovascular events at about the same rate as cigarette smoking, hypertension, and diabetes.

70. A paper published in the December 4, 2004 LANCET found, after analyzing 18 randomized controlled trials and 11 observational studies, that by the year 2000 these studies showed an increased risk of myocardial infarction from use of Vioxx and that it should have been withdrawn years earlier. Pfizer was aware of each of these studies and should not have advertised Bextra as generally safe.

71. An Australian study released in March 2005 analyzed results from all nineteen randomized controlled trials of COX-2 inhibitors published before May 2004 and found that those studies indicated that individuals taking COX-2 inhibitors, including Bextra, had a 60% higher chance of elevated blood pressure compared with those on a placebo.

72. Despite years of studies on COX-2 inhibitors, as well as disturbing new studies specifically analyzing the risks of Bextra, Defendants failed to take any action to protect the health and welfare of patients and instead continued to promote the CV safety of Bextra.

73. On April 7, 2005, the FDA requested that Defendants voluntarily withdraw Bextra from the market, stating:

> . . . the Agency has concluded that the overall risk versus benefit profile of Bextra is unfavorable. This conclusion is based on the potential increased risk for serious cardiovascular (CV) adverse events, which appears to be a class effect of non-steroidal anti-inflammatory drugs (NSAIDs) (excluding aspirin), an increased risk of serious skin reactions (e.g. toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme) compared to other NSAIDs, and the fact that Bextra has not been shown to offer any unique advantage over the other available NSAIDs.

FDA Alert for Healthcare Professionals, April 7, 2005.

74. Continuing, the FDA noted:

> Bextra has been demonstrated to be associated with an increased risk of serious adverse CV events in two short-term trials in patients immediately post-operative from coronary artery bypass graft (CAB G) surgery.... FDA has concluded that it is reasonable to extrapolate the adverse CV risk information for Bextra from the short-term CABG trials to chronic use given the fact that other COX2 selective NSAIDs have been shown in long-term controlled clinical trials to be associated with an increased risk of serious adverse CV events (e.g., death, MI, stroke), and the well described risk of serious, and often life-threatening gastrointestinal bleeding.... To date, there have been no studies that demonstrate an advantage of Bextra over other NSAIDs that might offset the concern about the[] serious skin risks, such as studies that show a GI safety benefit, better efficacy compared to other products, or efficacy in a setting of patients who are refractory to treatment with other products.

Id.

75. Pfizer agreed to suspend sales of Bextra, and Bextra has been withdrawn from the market as of April 7, 2005.

C. Marketing and Promotion

76. Despite knowing (i) that Bextra posed serious cardiovascular risks for anyone who took it, along with the risk of a death-causing skin disease, (ii) that Bextra provided no clinically proven improvement over pain relief for OA and RA, (iii) that Bextra was not indicated for the treatment of acute pain and (iv) that Bextra provided no clinically proven improvement for GI safety, Defendants made a business decision to push Bextra to market on claimed improvements in GI and CV safety, while downplaying its skin dangers.

77. Defendants initiated extensive marketing campaigns to convey the uniform message that Bextra provided effective pain relief without the gastrointestinal and cardiovascular side effects of other NSAIDs. Such claims were not permitted by the FDA. Defendants also falsely promoted Bextra as safe by downplaying or omitting the serious skin risks posed by use

of the drug. Defendants pursued this strategy to benefit from the assumption that, in the absence of information to the contrary, Bextra possessed the same skin dangers as traditional NSAIDs.

78. Defendants' advertising efforts included blitzing doctors' offices with literature and verbal presentations designed to convince both doctors and consumers that Bextra was a superior drug for treatment of osteo and rheumatoid arthritis and primary dysmenorrhea. They aggressively promoted Bextra as an improvement over older, less expensive NSAIDs, like naproxen and ibuprofen, claiming it had a lower risk of gastrointestinal side effects such as gastrointestinal ulcers and bleeding. Defendants did not promote or provide any balanced presentation as to Bextra having an unacceptably high risk of other side effects, such as heart attacks, strokes, unstable angina, cardiac clotting, hypertension, and severe skin reactions.

79. Such marketing efforts to physicians have become commonplace in recent years. Drug companies pay national and local "thought leaders" or "key opinion leaders," including local specialists, to speak at continuing medical education events that promote the use of expensive new drugs such as Bextra. In addition, drug companies - with Pfizer in the forefront - spent billions on "detailing" to physicians - i.e., having their sales representatives visit doctors in their offices, frequently bringing gifts and lunch, to "educate" doctors about their companies' drugs.

80. The deceptive marketing techniques that Pfizer employed through "thought leaders" are apparent in an internal summary document of a November 2001 advisory committee meeting regarding the marketing of Bextra. Even though Defendants received feedback at the meeting from its advisors that "CV concerns with Bextra seem real, considering: 92% of OA patients in study #047 developed hypertension. Hypertensive patients undergoing CABG have higher incidence of MI," they also received the following marketing feedback:

> Do not draw unnecessary attention to CABG data by communicating about it too much.

> . . .
>
> [It is] [h]ard to position Bextra for pain and Celebrex for arthritis, when labeling positions Bextra for arthritis not pain - marketing plan is out of sync with the label.
>
> . . .
>
> Physician education will be crucial to explain why Bextra should be used instead of other NSAIDs when the product has no pain indication. Pain data must be disseminated via medical education initiatives.
>
> . . .
>
> Publish BEXTRA acute pain abstracts soon and often. It sends a powerful message.

(emphasis added). Defendants clearly heeded this advice and did exactly as recommended by (1) downplaying any cardiovascular safety signals by not raising or avoiding negative data, even though such data was in sync with the cardiovascular risks noted in the Bextra label, (2) marketing Bextra for acute pain, an indication for which it was not approved, and (3) avoiding the limits placed on Bextra's marketing by the FDA labeling by providing one sided pain data to doctors under the guise of "medical education."

81. The Defendants marketed Bextra for use in the treatment of pain, contrary to its FDA approved labeling, directly to doctors. In a summary document of "Final Evaluations" from the 2002 National Consultant's Meeting for Orthopedic Surgeons organized by Defendants, participant responses to the question "which specific information presented did you find most compelling," included,

- Valde[coxib] used as pain med.
- Pain data - synergy of multimodal therapy
- Safety & efficacy of Celebrex & Bextra

. . .

- Gastrointestinal safety profile of COX-2 inhibitors

. . .

- Although Bextra doesn't have a pain indication, it is effective in pain management
- Use of Bextra as a pre-op adjunct and post op for management of pain. . .

The physician responses establish that Defendants were ignoring the FDA indications for Bextra and moving forward with their marketing strategy, falsely marketing Bextra as generally safe and effective especially for GI and promoting it for pain even though the FDA refused to approve it for the treatment of pain.

82. At meetings with analysts, Pfizer revealed its marketing strategy and the message it was conveying to medical providers for the use of Bextra, as reported in a December 21, 2001 report published in ESPIcom Business Intelligence Ltd:

> Pfizer also received regulatory approval for Bextra, a second generation Cox-2 inhibitor for the treatment of osteoarthritis (OA), rheumatoid arthritis (RA) and menstrual pain. Co-promoted with Pharmacia, Bextra is a new, once-daily option for people with OA and RA. It offers improved gastrointestinal toleration with no increase in renal or cardiovascular risk versus traditional NSAIDs.

83. In this and other press releases and promotional devices Defendants falsely promoted the GI and CV superiority of Bextra as compared to other NSAIDs.

84. Based on information supplied by Pfizer, the following appeared in the August 9, 2003, CHEMIST & DRUGGIST:

> Bextra is a new. .. Cox - 2 inhibitor from Pfizer indicated for treatment of symptoms of osteoarthritis and rheumatoid arthritis as well as dysmenorrhoea. In clinical trials it showed similar efficacy to maximum doses of naproxen, ibuprofen and diclofenac, but has a lower incidence of gastroduodenal ulcers than the traditional NSAIDs. Bextra contains valdecoxib, a Cox-2 enzyme inhibitor.

85. Based on information supplied by Pfizer the following appeared in COMMUNITY PHARMACY on July 21, 2003:

> Bextra (valdecoxib), from Phannacia, is a new cyclooxygenase-2 (Cox-2) selective inhibitor, indicated for the symptomatic relief of osteoarthritis (OA), rheumatoid arthritis (RA) and primary dysmenorrhoea. In the UK, 20 million people have an arthritic condition and up to pounds 920 million, excluding indirect costs, is spent annually on their care. Bextra offers a powerful alternative to maximum doses of the traditional non-steroidal anti-inflammatory drugs (NSAIDs), diclofenac, naproxen and ibuprofen in OA and RA, and a powerful alternative to naproxen sodium for those patients suffering pain associated with primary dysmenorrhoea, says the company. ***Additionally, being selective it largely avoids gastrointestinal side effects.*** (Emphasis added.)

86. The following was published at the request of Pfizer in THE PRACTIONER on July 7, 2003:

> **Bextra** is a fast-acting oral COX-2 selective inhibitor for the treatment of osteoarthritis, rheumatoid arthritis and primary dysmenorrhoea, and was developed to offer an alternative to maximum dose traditional **NSAIDs**. The recommended dose in arthritis is lO mg once- daily, although some patients may benefit from a 20mg dose daily. Patients suffering from menstrual cramps are recommended to take 40mg doses.

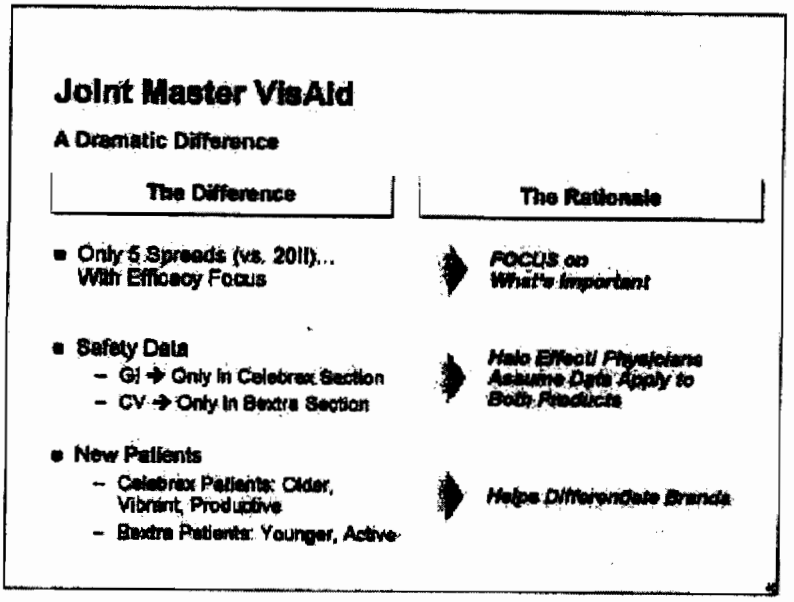
87. On or about May 19,2003, Pfizer issued the following statement:

> Pfizer Inc Receives Approval to Market New Oral COX-2 Inhibitor Bextra (Valdecoxib) in Europe
>
> Pfizer Now Offers the Widest COX-2 Inhibitor Portfolio
>
> NEW YORK, May 19 - Pfizer Inc said today that it has received approval to market Bextra(R) (valdecoxib) film coated tablets, the newest COX-2 selective inhibitor in its portfolio, in Europe for treatment of patients with pain and inflammation associated with osteoarthritis (OA), rheumatoid arthritis (RA) and primary dysmenorrheal (painful menstrual cramping).
>
> Valdecoxib received marketing authorization from the European Commission with labeling that is valid in all 15 European Union (EU) member states, and the approval will be extended to Norway and Iceland. This approval allows Pfizer to offer the widest portfolio of COX-2 selective inhibitors in Europe.

> "We are pleased with the ED Commission decision to approve Bextra and look forward to offering patients and physicians a new option for treating osteoarthritis, rheumatoid arthritis and primary dysmenorrheal," said Dr. Jack Watters, Pfizer's Vice President, Medical and Regulatory, Europe and Canada. "COX-2 selective inhibitors are an innovative class of medicines specifically developed to relieve pain and inflammation as effectively as widely used conventional non-steroidal anti-inflammatory drugs, ***while offering an improved upper gastrointestinal safety profile,***" he added. (Emphasis added.)

88. Each of the foregoing releases was designed to create demand for Bextra by those making decisions concerning the use of Bextra by patients. Each of the foregoing were just examples of dozens of such marketing ploys disseminated by Defendants.

89. Another of Defendants' marketing ploys was to detail Bextra along side of Celebrex, revealing only the positive data for each drug so that doctors would think that the positive data actually applied to both drugs. The Defendants referred to this marketing strategy as the "Halo Effect." The Halo Effect is contrary to the FDA approved labeling for both drugs in that it promoted each drug with data that had no scientific connection whatsoever to that drug. Defendants' employment of the Halo Effect shows a clear lack of fair balance in the Defendants' detailing methods - ignoring the risks of one drug and touting its benefits. As revealed in the sales training presentation below, the Halo Effect was taught as a technique for marketing both drugs. Such selective presentation of safety data was contrary to the FDA approved labeling.



90. Another of Defendants' marketing and promotional devices that was deceptive and contrary to its FDA approved labeling was the funding of research designed to falsely produce positive outcomes with Bextra usage. These findings were then published in medical journals and distributed via press releases and other public relations techniques to medical and non-medical media, targeted at doctors, the public and others in the drug purchasing decision chain. During the Class Period, these paid researchers touted the safety of Bextra. For example, the following doctor was quoted in a Pharmacia press release, dated November 27, 2002, as follows:

> "Our analysis suggests that valdecoxib shows no greater incidence of cardiovascular events than either naproxen or placebo," said lead author Andrew Whelton, M.D., adjunct professor of Medicine, Johns Hopkins University, Baltimore, Maryland. "While more data are necessary to confirm this conclusion, our findings suggest that valdecoxib demonstrates a cardiovascular safety profile similar to that of placebo or naproxen."
>
> According to Whelton, "Whether patients were or were not taking aspirin did not significantly impact the incidence of serious adverse events."

91. Such a claim is not permitted by the FDA label or within the scope of FDA approval.

92. Another example of Defendants' deceptive marketing is the republication, in a press release issued on August 1, 2002, of the results of a study in the JOURNAL of OBSTETRICS AND GYNECOLOGY purporting to show that Bextra was more effective than Naproxen for treatment of pain during menstruation. The study compared Bextra 40 mg twice daily (BID) as needed, Bextra 20 mg BID as needed, naproxen sodium 550 mg BID as needed, to placebo for up to 3 days for the treatment of pain associated with menstruation (dysmenorrheal). The maximum dose of Bextra approved by the FDA for the treatment of primary dysmenorrhea was up to 20 mg BID per day. On every measure of pain relief, naproxen sodium 550 mg provided better pain relief than Bextra 20 mg BID (some of the differences achieved statistical significance). Furthermore, patients taking Bextra 20 mg BID experienced more than twice as many of the most common side effects as did the patients taking naproxen sodium 550 mg BID. In other words, Bextra provided inferior pain relief, caused more side effects, and cost far more than naproxen sodium - it's hard to understand how this data could be used to make the case that Bextra was the superior choice - but that is just what Defendants did. SClREX Clinical Research Center, a company owned in part by OMNICON, one of the largest advertising agencies, was hired by Pfizer to conduct this study. Pfizer reprinted parts of the study, omitting the known risks of cardiovascular and skin disorders. Again, any claims of pain superiority over other drugs was not permitted by the FDA label.

93. Defendants also used SCIREX, to promote Bextra via an article and an accompanying continuing education quiz published in the JOURNAL OF THE AMERICAN DENTAL ASSOCIATION. The study, featured by Pharmacia in a press release dated May 8, 2002, purported to show Bextra's superiority for use in pain relief. No disclosure was made of the researchers' financial ties to Pharmacia or to the known adverse effects associated with Bextra. One of the three scientific reviewers of the paper - an associate editor of the journal- told the NY Times that,

had he known that Bextra had not been approved by the FDA for relief of dental pain, he would have recommended the paper be rejected. As it was, the paper was published in the journal, along with a continuing education quiz to reinforce the message that Bextra is helpful for post-dental surgery pain, an indication for which Bextra was not approved.

94. These and similar studies helped increase the acceptance of Bextra by medical and dental providers.

95. The Defendants also targeted consumers directly with false marketing claims regarding Bextra. Some of the methods they used to reach consumers included leaving patient directed brochures at doctors' offices and providing marketing materials to doctors that could be distributed to their patients. Defendants also maintained websites and a toll free telephone number that conveyed misleading information regarding the safety and efficacy of Bextra. As noted in an internal memorandum, "there are several successful programs in the market now with proven value in generating consumer demand for Bextra (e.g. TIME/PEOPLE Coverwrap MD Office program, PERFORM magazine, In Office brochure) and this POA we will shortly roll out the very successful unbraded." "On the Road to Pain Relief' long format (30min) direct response TV ad."

96. As referenced above, the use of "unbranded" advertising is another all too common and sophisticated method of advertising that Defendants used to market Bextra to consumers. It is also a method of advertising that Defendants hoped would shield them from responsibility for false claims conveyed. As one of Pfizer's sales managers describes in October 2004, immediately after the withdrawal of Vioxx, "[w]e are currently running an unbranded long-format ad as well as a 60-second ad about arthritis symptoms and appropriate treatment options. Consumers who respond to these advertisements receive branded information on

CELEBREX and/or Bextra." Thus, the "unbranded" advertisements were clearly used to market Celebrex and Bextra directly to consumers.

97. After the withdrawal of Vioxx, and just one day before the Celebrex APC trial was halted because of CV safety concerns, Defendants produced a document entitled "US Field Force Selling Objections and Answers." The document warns that it is "Company confidential," "for internal use only," "DO NOT DETAIL" and "This document is provided to you for your background information only," but then goes on to describe how to respond to "objections health professionals may raise regarding Bextra." The first question and answer highlight how the Bextra sales force was trained to promote the CV and GI safety of Bextra, even in the face of scientific evidence to the contrary:[2]

> Q1: How can I prescribe Bextra when patients with arthritis often have increased CV risk?
>
> A: Bextra still can be administered safely to patients with arthritis. In a large pooled analysis of 10 arthritis trials in which almost half the patients had at least 1 coronary risk factor, there were no apparent differences detected in the serious CV thrombotic event rates between patients receiving Bextra, placebo, and nonspecific NSAIDs. In this analysis, 13% of patients were taking daily low dose aspirin, with no increase in CV risk with Bextra. While Bextra is contraindicated for the treatment of postoperative pain following coronary artery bypass graft, or CABG, surgery, it remains an effective and safe treatment for vast number of patients with arthritis who need pain relief along with superior GI safety.

98. Thus, as reflected above, the Defendants instructed their sales force to market Bextra in a manner that the FDA had not approved and in direct contradiction to the approved FDA labeling.

99. In another "objection response" in the same document, Defendants again tout the GI superiority of Bextra, again in direct contradiction to the FDA approved labeling:

[2] The entire document from which this is excepted is attached hereto as Exhibit 1.

> Q 1: How can I prescribe Bextra when it is so difficult to get reimbursement for COX-2 specific inhibitors?
>
> The formulary status for Bextra has not changed dramatically. And several managed care plans may be using the latest developments as a reason to question the clinical value and appropriateness of the COX-2 specific inhibitor class. However, managed care plans do realize that only physicians know the appropriate therapy for their patients. Because the risk of GI bleeding remains a serious issue with nonspecific NSAIDs, treatment guidelines still stress COX-2 specific inhibitors as first-line treatment for patients at GI risk.
> Consequently, managed care plans will continue to reimburse for drugs such as COX-2 specific inhibitors as long as physicians confidently affirm that these medications are medically necessary and appropriate for their patients.

100. Defendants' false promotions of the cardiovascular safety and superiority of Bextra are evident in the following advertisement. In the advertisement, doctors are falsely reassured that they can safely prescribe Bextra because of its "established CV profile," even though no such established CV profile existed and no such profile appears in the FDA approved labeling. Furthermore, the bold statement "Prescribe CELEBREX and BEXTRA With Confidence" implies that absolutely none of the risk information contained in the FDA approved labeling even exists. Such advertising is deceptive and contrary to the FDA approved label for Bextra.[3]

Prescribe CELEBREX and BEXTRA With Confidence

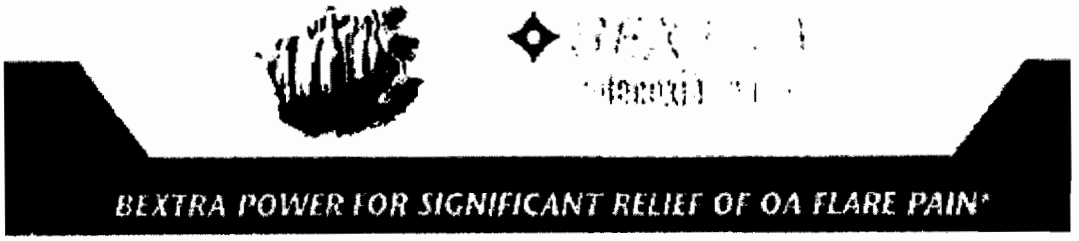
CV safety with the efficacy your patients may need

CELEBREX and BEXTRA have an established CV profile[1]

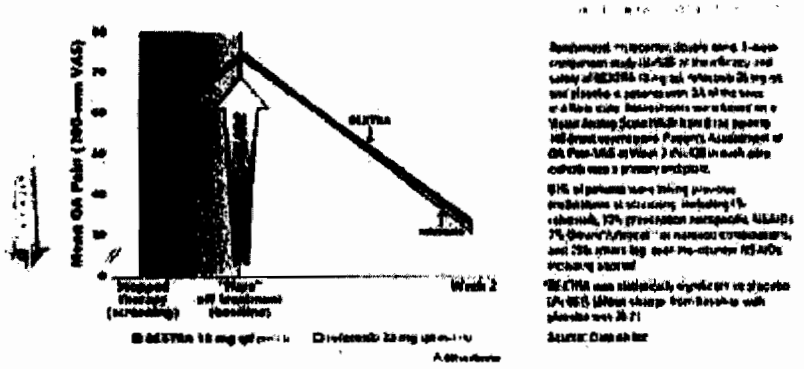
CELEBREX and BEXTRA both provide joint pain relief with established CV safety[1,4]

[3] The excerpt above appears as bates number Cele NDA 20-99800022356 of Defendants' document attached hereto as Exhibit 2.

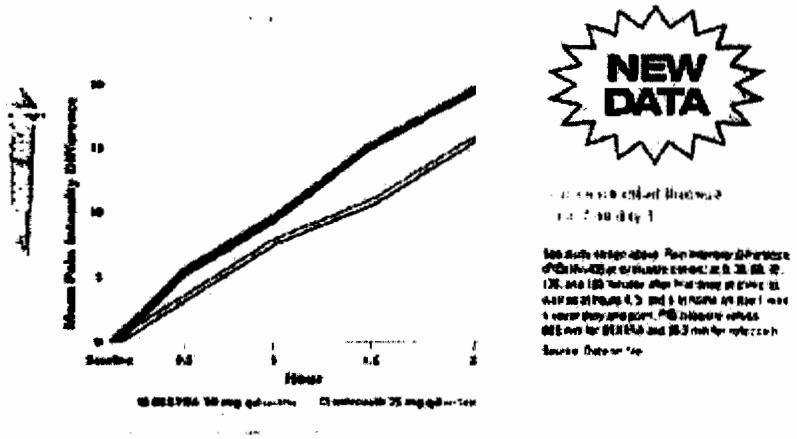
101. The Defendants strategically placed comments on the CV safety of Bextra with claims of superior efficacy. In the following advertisement, Defendants imply that there is no CV risk with Bextra because in unspecified "clinical trials," the incidence of CV events is similar to a placebo. Such a claim lacks fair balance, since it implies that there are no clinical trials in which CV events are higher as compared to placebo - which there were - and is in direct contradiction to the FDA approved labeling. The footnote after the false CV claim leads a reader to the dead end "Data on file, Pfizer Inc., New York, NY," and hence, does not cure the deceptive presentation.[4]



BEXTRA 10 mg power vs rofecoxib 25 mg compared with baseline

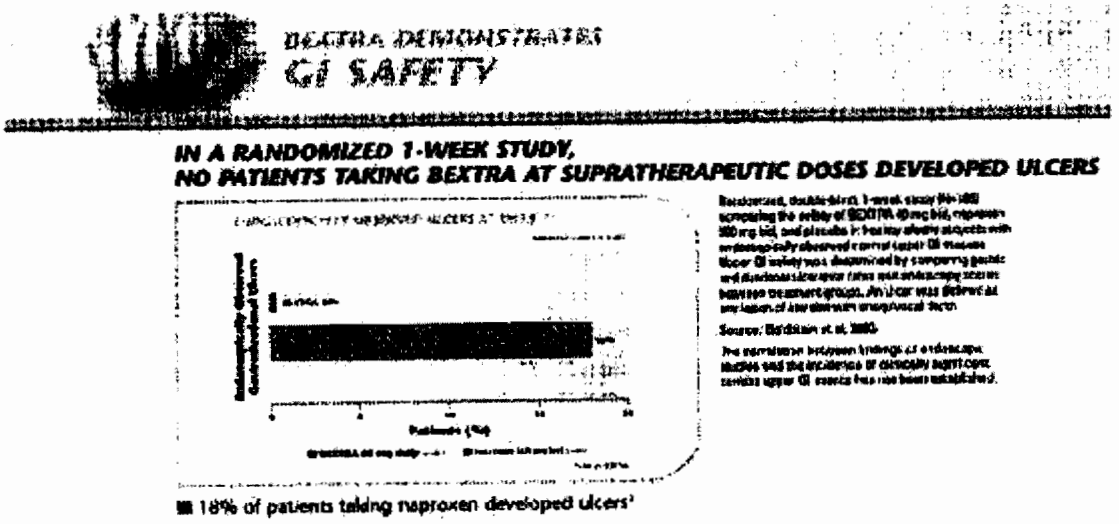


[4] The referenced excerpt appears at bates number Bex NDA 21-341 00013129 of Defendants' document attached hereto as Exhibit 3.

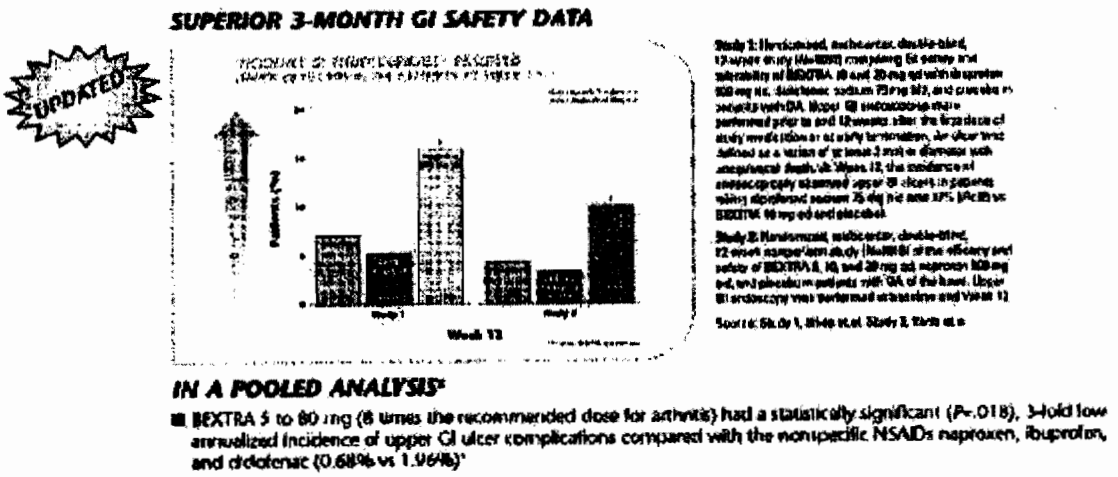


In clinical trials, incidence of CV adverse events with BEXTRA 10 to 20 mg was similar to placebo[1]

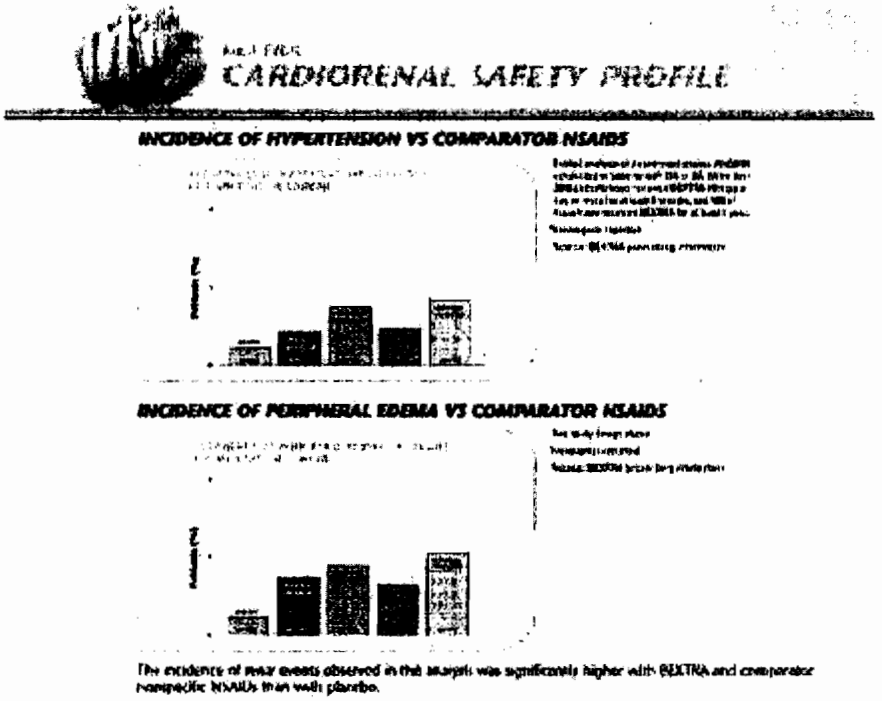
102. In this December 2004 ad, Bextra was falsely promoted, contrary to its FDA approved labeling, as having "SUPERIOR 3-MONTH GI SAFETY DATA" and deceptive data was presented as "POOLED ANALYSIS" in support of that claim. In a January 2001 letter, however, the FDA scolded Defendants about the continuous onslaught of misleading advertisements and advertising methods, stating, "[w]e are not aware of any evidence showing that Celebrex or Bextra has superior effectiveness to non-selective NSAIDs."[5]



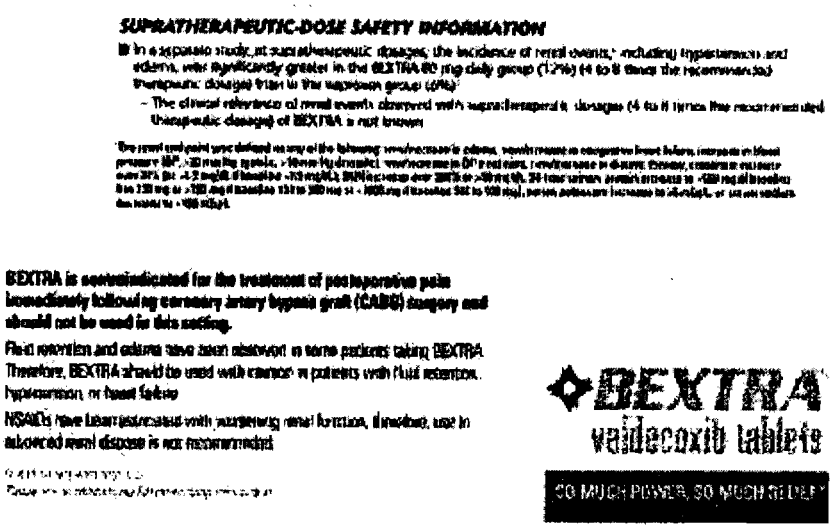
[5] The image above appears at bates number Litwac-A 10000617953 in Defendants' document attached hereto as Exhibit 4.



103. The same detailing brochure contains this false pronouncement of the "CARDIORENAL SAFETY PROFILE" of Bextra. The graphic used include deceptive pooled analyses of data and includes partial and small print risk information that fails to present a fair balance of the risks associated with Bextra as detailed in its FDA approved labeling.[6]



[6] The image above appears at bates number Litwac-A 10000617955 of Defendants' document attached hereto as Exhibit 5.



104. Each of the foregoing advertisements was designed to create demand for Bextra by those making decisions concerning the use of Bextra by patients. Each of the foregoing were just examples of dozens of such marketing ploys disseminated by Defendants either orally to doctors or in written material.

D. Risks Posed by Bextra

105. Despite the effectiveness of their advertising campaigns, Defendants' false promotion of Bextra by touting it as GI and CV safe and downplaying its risk of severe skin reactions did not quell concerns about selective COX-2 inhibitors in the medical community.

106. In 1997, the link between COX-2 inhibition, prostacyclin levels, and blood clotting was receiving attention in medical journals.

107. In 1998, independent doctors established a link between selective COX-2 inhibitors and increased blood clotting, and suggested that these drugs would cause an increase in clot-related cardiovascular events. These doctors suggested that these drugs should not be given to patients with known cardiovascular disease, and that patients taking these drugs would have to be monitored for cardiovascular complications.

108. The cardiovascular safety of selective COX-2 inhibitors was directly challenged in August 2001, when independent doctors from the Cleveland Clinic published a meta-analysis of the CLASS trial that concluded these drugs posed an increased risk of adverse cardiovascular events compared to naproxen, a traditional NSAID.

109. Despite the mounting evidence that Bextra caused or exacerbated clot-related cardiovascular disorders, Defendants continued to issue uniformly misleading advertisements and promotional materials touting Bextra as being safe and more effective than traditional NSAIDs for all patients, without regard for gastrointestinal and cardiovascular risks.

110. Defendants' advertising and packaging materials for Bextra are uniformly fraudulent and misleading because they falsely promote Bextra as safe, even though Bextra was known to pose risks of gastrointestinal adverse events, heart attacks, strokes, unstable angina, cardiac clotting, hypertension, and severe skin reactions.

111. At the Joint Meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee, the Committee concluded that "no clear data shows GI benefit for Celebrex and Bextra." The Committee noted that the GI benefits are "less than first reported," referring to reports by Defendants and others regarding trials they had coordinated purporting to show GI benefits.

E. Defendants' Continued Unlawful Marketing Campaign Caused Overcharges to End Payors for Bextra

112. As a result of Defendants' claims, Plaintiff purchased and/or paid for Bextra even though a monthly supply was much more expensive than other NSAIDs.

113. To justify the disparity of Bextra's pricing as compared to other NSAIDs and to ensure that physicians would prescribe and that End-Payors would purchase the drug, Defendants misrepresented the safety and efficacy of Bextra and suppressed the risks, dangers, and disadvantages of the drug. Consequently, Bextra captured a large market share of anti-

inflammatory drugs prescribed for and used by patients. In 2004 alone, sales of Bextra exceeded $1.2 billion, despite the significantly higher cost of Bextra as compared to other pain relievers in the same family of drugs.

114. Defendants' deceptive and misleading marketing campaign concealed, omitted, and suppressed information that resulted in overcharges to consumers and third-party payors, such as Plaintiff, for, in whole or in part, the costs of Bextra. Millions of End-Payors, including consumers and third-party payors, have already paid for, and/or purchased and consumed Bextra at prices based on the proposed wholesale price, which was about one hundred times the cost of a generic aspirin. These End- Payors did not get the benefit of the bargain that Defendants held out to them, and as a result End-Payors paid more than they would have or should have because Bextra was promoted and advertised as a premium drug with reduced side effects for the purpose of deceiving consumers and End-Payors about Bextra's adverse gastrointestinal, cardiovascular, cerebrovascular and cardiorenal effects. Had the truth been told and Bextra not been promoted contrary to its approved labeling it would not have been placed on formularies and not been paid for by End Payors.

FRAUDULENT CONCEALMENT

115. Plaintiff did not discover, and could not discover through the exercise of reasonable diligence, that Defendants were falsely over promoting the safety and efficacy until April 7, 2005, when Pfizer withdrew Bextra from the market. Defendants conducted its unlawful activities in secret, concealed the nature of their unlawful conduct, and attempted to confine information concerning the adverse effects of Bextra. Defendants attempted to withhold such information from Plaintiff, the medical community, regulators, and the public. Defendants fraudulently concealed its activities through various means and methods designed to avoid detection.

116. Plaintiff could not have discovered Defendants' unlawful conduct at an earlier date through the exercise of reasonable diligence because Defendants actively and purposefully concealed their unlawful activities.

117. Defendants engaged in a successful, illegal fraud on consumers, third-party payors and the general public, by which they deliberately and affirmatively misrepresented the risks, dangers, defects, and disadvantages of Bextra, in at least the following respects:

a. By falsely promoting the safety and efficacy of Bextra to Plaintiff, the medical community, and the public in a manner that exceeded the scope of FDA approval;

b. By omitting adverse event risks from its promotions of Bextra to the Plaintiff, the medical community, and the public in a manner that made its promotion not fairly balanced and inconsistent with the express label or the intent of the label;

c. By agreements among senior Pfizer and Pharmacia officials in meetings and in communications not to discuss publicly, or otherwise reveal, the totality of the adverse effects caused by Bextra, Defendants' concealment of those adverse effects, and the nature and substance of other acts and communications in furtherance of Defendants' illegal scheme; and

d. By giving false and pretextual reasons for the existence of apparent adverse effects in studies of COX-2 drugs, including, for example, by claiming that naproxen's cardioprotective effect was responsible for a noted increase in cardiovascular events in the VIGOR study in Vioxx versus naproxen patients, when, in fact, Vioxx is another COX-2 inhibitor which was the cause of the reported increased incidence of cardiovascular effects.

118. As a result of Defendants' fraudulent concealment, Plaintiff purchased and/or paid for Bextra and could not reasonably have discovered Defendants' misconduct regarding Bextra prior to April 7, 2005. Plaintiff therefore asserts the tolling of any applicable statute of limitations affecting the rights of action of Plaintiff.

COUNT I

VIOLATION OF THE MISSOURI MERCHANDISING PRACTICES ACT
MO. STAT. REV. § 407.010, *et seq.* – DECEPTIVE ACTS and PRACTICES

119. Plaintiff hereby restates and re-alleges each and every allegation set forth in above, with the same force and effect as if herein repeated and set forth at length.

120. The Purpose of The Missouri Merchandising Practices Act, Mo. Stat. Rev. § 407.010, *et seq.*, ("MMPA"), in part, is to protect consumers from suppliers who commit deceptive practices. Mo. Stat. Rev. § 407.020. The Court must construe the MMPA liberally to promote its purpose. *Id.*

121. Defendants supplied Bextra, either by manufacture, distribution, or sales of the drug, even if only indirectly to Plaintiff, its' insured, and/or plan members.

122. The MMPA states that no supplier shall engage in any deceptive act or practice in connection with a consumer transaction. Mo. Stat. Rev. § 407.020.

123. Plaintiff's purchases and/or payments made with respect to Bextra from November 16, 2001 to April 7, 2005, constitute consumer transactions within the meaning of the MMPA.

124. The MMPA provides, in pertinent part, that:

> "The act, use or employment by any person of any deception, fraud, false pretense, false promise, misrepresentation, unfair practice or the concealment, suppression, or omission of any material fact in connection with the sale or advertisement of any merchandise in trade or commerce or the solicitation of any funds for any charitable purpose, as defined in section 407.453, in or from the state of Missouri, is declared to be an unlawful practice. The use by any person, in connection with the sale or advertisement of any merchandise in trade or commerce or the solicitation of any funds for any charitable purpose, as defined in section 407.453, in or from the state of Missouri of the fact that the attorney general has approved any filing required by this chapter as the approval, sanction or endorsement of any activity, project or action of such person, is declared to be an unlawful practice. Any act, use or employment declared unlawful by this subsection violates this subsection whether committed before, during or after the sale, advertisement or solicitation." Mo. Stat. Rev. § 407.020.1

And further provides, in pertinent part, that:

> "Any person who purchases or leases merchandise primarily for personal, family or household purposes and thereby suffers an ascertainable loss of money or property, real or personal, as a result of the use or

> employment by another person of a method, act or practice declared unlawful by section 407.020, may bring a private civil action in either the circuit court of the county in which the seller or lessor resides or in which the transaction complained of took place, to recover actual damages. The court may, in its discretion, award punitive damages and may award to the prevailing party attorney's fees, based on the amount of time reasonably expended, and may provide such equitable relief as it deems necessary or proper." Mo. Stat. Rev. § 407.025.

125. Defendants' marketing and sales activities with regard to Bextra between November 16, 2001 and April 7, 2005, constituted deceptive acts and practices in violation of Mo. Stat. Rev. § 407.020.

126. Defendants willfully omitted, suppressed, concealed, and/or failed to state material facts concerning the dangers and risks associated with the use of Bextra, including but not limited to the risks of heart disease and cardiovascular injury. Further, Defendants willfully downplayed and/or understated the serious nature of the risks associated with Bextra use in order to increase the sales of Bextra.

127. In their interaction with the FDA regarding the safety and efficacy of Bextra, Defendants falsely and deceptively misrepresented or willfully omitted, suppressed, or concealed facts of such materiality that, had the FDA known of such facts, the drug would never have been approved and no physician would have been able to prescribe this drug to Plaintiff's plan members.

128. Defendants knew or should have known (or would have known had appropriate testing been done) that use of Bextra caused serious and potentially life-threatening side effects of cardiovascular injury, especially when used for extended periods of time.

129. Defendants willfully engaged in calculated silence despite their knowledge to the growing public acceptance of misinformation and misrepresentations regarding both the safety and efficacy of the use of Bextra, and did so because the prospect of significant future profits outweighed their concern regarding health and safety issues, all to the significant detriment of the public and Plaintiff.

130. Many safe and less expensive indigestion agents were available to plan members treated with Bextra.

131. Defendants knowingly and intentionally touted the quality and standards of Bextra that they knew were materially different from their representations of the drug, precluding Plaintiff from making informed decisions with respect to whether or not Bextra should be a covered prescription medication.

132. Defendants willfully downplayed the side effects and/or provided misinformation about adverse reactions and potential harms from Bextra, and succeeded in persuading large segments of the relevant consumer market to request, and large segments of the medical community to prescribe Bextra, despite both the lack of efficacy and the presence of significant dangers, as set forth herein.

133. Defendants' success in persuading large segments of the relevant consumer market to request, and large segment of the medical community to prescribe Bextra, caused Plaintiff to purchase and/or pay for Bextra prescriptions on behalf of its plan members.

134. Defendants had a clear post-manufacturing duty to warn, which arose when they knew, or with reasonable care should have known, that Bextra was fatal or injurious.

135. Defendants' actions set forth herein constitute willful concealment, suppression, or omission of material facts, made with the intent that others would rely upon such concealment, suppression or omission, in connection with the sale and marketing of Bextra in violation of Mo. Stat. Rev. 407.010 *et seq*.

136. Additionally, Defendants' use of various media and detail men to advertise Bextra involved willful oral and/or written representations of exaggeration, falsehood, innuendo or ambiguity as to material facts and therefore constituted deceptive acts or practices as defined by Mo. Stat. Rev. 407.010 *et seq*.

137. In paying for plan members' prescriptions for Bextra, at all times relevant, Plaintiff reasonably relied on Defendants' misleading marketing and advertising scheme.

138. As a proximate result of the aforesaid violations of the MMPA, Plaintiff has suffered ascertainable loss - economic loss that includes the purchase price of the drugs, and is entitled to reasonable attorney fees, and statutory penalties, for each individual violation of the MMPA, for which Defendants, jointly and severally, are liable to Plaintiff for their actual damages.

COUNT II

UNJUST ENRICHMENT

139. Plaintiff hereby restates and re-alleges each and every allegation set forth above, with the same force and effect as if herein repeated and set forth at length.

140. Plaintiff, having purchased and/or made payments with respect to its insured and plan members' prescriptions for Bextra, have unjustly enriched Defendants.

141. In order to maintain sales and profits, Defendants knowingly and intentionally withheld material facts that would have informed Plaintiff and the medical community that Bextra's risks outweighed its benefits and that it should not have been a covered prescription medication available to plan members.

142. As a result, the sales of Bextra provided ill-gotten gains for Defendants at the expense of Plaintiff, which Defendants cannot justify retaining.

143. As a direct and proximate result of the Defendants' acts, omissions and conduct as set forth above, Plaintiff is entitled to an award of a refund, restitution, and incidental economic losses, including the purchase price paid for the drug Bextra.

COUNT III

IMPLIED WARRANTY

144. Plaintiff hereby restates and realleges each and every allegation set forth above, with the same force and effect as if herein repeated and set forth at length.

145. Defendants are merchants and are in the business of selling selective COX-2 inhibitor drugs such as Bextra.

146. Bextra was not of merchantable quality and was not fit for its intended use, because it causes increased risk of serious cardiovascular and cerebrovascular adverse events, including heart attacks, strokes and other serious and harmful adverse health effects.

147. Defendants breached their implied warranty that Bextra was of merchantable quality and fit for such use in violation of Mo. Stat. Rev. § 400.2-314, *et seq*.

148. As a proximate cause of Defendants' breach of warranty, Plaintiff suffered ascertainable losses, injuries and damages as specified herein in an amount to be determined at trial.

149. In marketing and selling Bextra, Defendants impliedly warranted that Bextra provided effective pain relief without the gastrointestinal side effects of traditional NSAIDs.

150. In marketing and selling Bextra, Defendants intentionally mislead purchasers to believe, and impliedly warranted, that Bextra was cardiovascualarly safer than other NSAIDs and less dangerous to the skin than traditional NSAIDs.

151. In reality, Bextra failed to provide effective pain relief without the gastrointestinal side effects of traditional NSAIDs. In fact, Bextra caused or exacerbated cardiovascular and potentially fatal skin injury far more often than traditional NSAIDs, and even more often than other selective COX-2 inhibitor drugs. Accordingly, for these and other reasons, Bextra was not fit for the purposes for which it was sold and used, and it does not pass without objection in the trade.

152. Defendants did not effectively disclaim or otherwise limit their implied warranty of merchantability with respect to Bextra. Therefore, Defendants breached the implied warranty of merchantability as to Plaintiff.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff pray that:

A. Plaintiff be granted an award of damages in such amount to be determined at trial, with treble damages as provided by law;

B. Plaintiff be granted an award of punitive damages in such amount to be determined at trial;

C. Plaintiff recovers its costs of suit, including reasonable attorneys' fees and expenses as provided by law; and

D. Plaintiff be granted an award of damages in such amount as necessary by law for each violation of the MMPA; and such other, further, and different relief as the nature of the case may require or as may be determined to be just, equitable, and proper by this Court.

Respectfully submitted,

Thomas P. Cartmell MO #45366
Thomas J. Preuss MO #54923
Christopher L. Schnieders MO #57725
WAGSTAFF & CARTMELL LLP
4740 Grand Avenue, Suite 300
Kansas City, MO 64112
(816) 701-1100
FAX (816) 531-2372

J. Scott Bertram MO #23715
Benjamin A. Bertram MO #56945
BERTRAM & GRAF, LLC
9229 Ward Parkway, Suite 225
Kansas City, MO 64114
(816) 523-2205
FAX (816) 523-8258

Michael L. Hodges KS #09860
HODGES LAW FIRM
13420 Santa Fe Trail Dr.
Lenexa, KS 66215
(913) 888-7100
FAX (913) 888-7388

John O'Mara MO#41835
5770 Mexico Road
St. Peters, Missouri 63376
636.757.1700 Main
636.757.0198 Fax

J. Mark Kell MO#26413
5770 Mexico Road
St. Peters, Missouri 63376
636.757.1700 Main
636.757.0198 Fax

Gerald B. Taylor
THE TAYLOR LAW FIRM
7208 Fairwoods Place
Montgomery, AL 36117
334-775-1025
FAX 334-775-1022

J. Paul Sizemore
GIRARDI & KEESE
1126 Wilshire Boulevard
Los Angeles, CA 90017
213-977-0211
FAX 213-481-1554

Steven R. Maher
MAHER, GUILEY AND MAHER, PA
631 West Morse Boulevard, Suite 200
Winter Park, FL 32789
407-839-0866
FAX 407-425-7958

ATTORNEYS FOR PLAINTIFF